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10/583,860	05/21/2007	Takashi Nishimura	3691-0133PUS1	8593

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

NOTIFICATION DATE	DELIVERY MODE
09/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,860	NISHIMURA ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6,14 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-13 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 May 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-12-06 & 4-23-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I, claims 1-5, 7-13 and 15-17 and specie WT1, in the reply filed on 6-9-08 is acknowledged. The traversal is on the ground(s) that groups I and II should be examined together because common technical feature is reflected, such as claims is generic to both groups. This is not found persuasive because the putative special technical feature common to groups I-IV is the Th cells or both Th1 and Tc1 cells that having a nonspecific antitumor activity and the impartation of antigen specificity to the cells. However, there is no special technical feature common to groups I and II that has been contributed by the instant invention over the prior art in view of the cited references Tsuji et al., April 2003 (Cancer Science, Vol. 94, No. 4, p. 389-393) and Ohmi et al., 1999 (Cancer Immunology, immunotherapy, Vol. 48, p. 456-462).

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 6, 14 and 18-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6-9-08.

Claims 1-21 are pending. Claims 1-5, 7-13 and 15-17, and species WT1 are under consideration.

Claim Objections

3. Claims 7 and 8 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim shall not serve as a basis for any other multiple dependent claim. See MPEP § 608.01(n). Claim 5 is a multiple dependent claim, and claims 7 and 8, which are multiple dependent claims, depend from claim 5. Claim 13 is a multiple dependent claim, and claims 15-17, which are multiple dependent claims, depend from claim 13. Accordingly, the claims 7, 8 and 13-17 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5, 7-13 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "Th" in claim 1 is vague and renders the claim indefinite. The term "Th" is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 2-5, 7 and 8 depend from claim 1 but fail to clarify the indefiniteness.

The term "TCR" in claim 2 is vague and renders the claim indefinite. The term "TCR" is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 5, 7 and 8 depend from claim 2 but fail to clarify the indefiniteness.

The phrase "class I-restricted TCR" in claim 3 is vague and renders the claim indefinite. It is unclear what kind of TCR is "class I-restricted TCR". It is unclear what "class I-restricted"

means. The specification fails to specifically define the phrase "class I-restricted". Claims 5, 7 and 8 depend from claim 3 but fail to clarify the indefiniteness.

The phrase “class II-restricted TCR” in claim 4 is vague and renders the claim indefinite. It is unclear what kind of TCR is "class II-restricted TCR". It is unclear what "class II-restricted" means. The specification fails to specifically define the phrase "class II-restricted". Claims 5, 7 and 8 depend from claim 4 but fail to clarify the indefiniteness.

The term “WT1” in claim 5 is vague and renders the claim indefinite. The term “WT1” is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 7 and 8 depend from claim 5 but fail to clarify the indefiniteness.

The term “Th1” in claim 9 is vague and renders the claim indefinite. The term “Th1” is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 10-13 and 15-17 depend from claim 9 but fail to clarify the indefiniteness.

The term “Tc1” in claim 9 is vague and renders the claim indefinite. The term “Tc1” is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 10-13 and 15-17 depend from claim 9 but fail to clarify the indefiniteness.

The term “TCR” in claim 10 is vague and renders the claim indefinite. The term “TCR” is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 13 and 15-17 depend from claim 10 but fail to clarify the indefiniteness.

The phrase “class I-restricted TCR” in claim 11 is vague and renders the claim indefinite. It is unclear what kind of TCR is "class I-restricted TCR". It is unclear what "class I-restricted" means. The specification fails to specifically define the phrase "class I-restricted". Claims 13 and 15-17 depend from claim 11 but fail to clarify the indefiniteness.

The phrase "class II-restricted TCR" in claim 12 is vague and renders the claim indefinite. It is unclear what kind of TCR is "class II-restricted TCR". It is unclear what "class II-restricted" means. The specification fails to specifically define the phrase "class II-restricted". Claims 13 and 15-17 depend from claim 12 but fail to clarify the indefiniteness.

The term "WT1" in claim 13 is vague and renders the claim indefinite. The term "WT1" is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Claims 15-17 depend from claim 13 but fail to clarify the indefiniteness.

The phrase "by transducing a gene for a TCR…" in claims 2 and 10 is vague and renders the claim indifnite. It is unclear what is being transduced with the gene for a TCR.

The phrase "by transducing a gene for a class I-restricted TCR…" in claims 3 and 11 is vague and renders the claim indefinite. It is unclear what is being transduced with the gene for a class I-restricted TCR.

The phrase "by transducing a gene for a class II-restricted TCR…" in claims 4 and 12 is vague and renders the claim indefinite. It is unclear what is being transduced with the gene for a class II-restricted TCR.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Ohmi et al., 1999 (Cancer Immunology, immunotherapy, Vol. 48, p. 456-462).

Claim 1 is directed to a process of preparing cells for cell therapy comprising inducing Th cells having a nonspecific antitumor activity and imparting antigen specifically to the Th cells.

Ohmi reports Th1 or Th2 cells were induced from naïve Th cells obtained from ovalbumin-specific T cell receptor (TCR) transgenic mice. Those T cells are antigen-nonspecific. However, co-culturing the Th1 cells with bispecific antibody consisting of anti-(mouse CD3) mAb and anti-(human cErbB-2) mAb results in Th1 cells that show antitumor activity in vivo against human C-erbB-2 positive tumor cells implanted in nude mice (e.g. abstract). Thus, claim 1 is anticipated by Ohmi.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-5, 7-13 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuji et al., April 2003 (Cancer Science, Vol. 94, No. 4, p. 389-393) in view of Gaiger et al., 2008 (US Patent No. 7323181 B2) and Nishimura, Takashi, 2000 (Cancer Treatment and Host, Vol. 12, No. 4, p. 363-373, IDS-CL).

Claim 1-5, 7 and 8 are directed to a process of preparing cells for cell therapy comprising inducing Th cells having a nonspecific antitumor activity and imparting antigen specifically to the Th cells. Claim 2 specifies transducing a gene for a TCR that recognize a cancer-associated antigen. Claims 3 and 4 specify transducing with class I-restricted TCR gene and class II-restricted TCR gene, respectively. Claim 5 specifies the cancer-associated antigen is WT1. Claims 7 and 8 specify further purifying the Th cells to which antigen specificity has been imparted by using antibody-bearing magnetic beads. Claim 9-13 and 15-17 are directed to a process of preparing cells for cell therapy comprising inducing Th1 cells and Tc1 cells having a nonspecific antitumor activity and imparting antigen specifically to the Th1 cells and Tc1 cells. Claim 10 specifies transducing a gene for a TCR that recognize a cancer-associated antigen. Claims 11 and 12 specify transducing with class I-restricted TCR gene and class II-restricted TCR gene, respectively. Claim 13 specifies the cancer-associated antigen is WT1. Claims 15 and 16 specify further purifying the Th1 cells and Tc1 cells to which antigen specificity has been imparted by using antibody-bearing magnetic beads. Claim 17 specifies further comprising a step of mixing the separated Th1 cells and Tc1 cells in any given proportion.

Tsuji discloses preparation of nonspecific Tc1 cells, naïve CD8+ T cells from C57BL/6 mouse spleen and activation of those cells by 2ug/ml plate bound anti-CD3 mAb under Tc1, Tc2 or neutral condition (e.g. p. 389, right column). Antigen-nonspecific CD8+ T cells were polyclonally expanded in the presence of IL-2, Th1 cytokines (IFN-gamma and IL-12) and anti-IL-4 mAb. The polyclonally activated CD8+ cells were transduced by retrovirus expressing 2C TCR alpha or 2C TCR beta chain to generate antigen-specific cytotoxic T lymphcytes (CTL). The 2C-TCR gene-modified antigen specific Tc1 cells exhibit antitumor activity both in vitro and in vivo (e.g. abstract).

Tsuji does not specifically teach transducing cells with gene for class II-restricted TCR, transducing both Th1 and Tc1 cells, or using cancer-associated antigen WT1. Tsuji also does not specifically teach separating the Th cells or Th1 and Tc1 cells with antibody-bearing magnetic beads or mixing separated Th1 cells and Tc1 cells in any proportion.

Gaiger teaches that "T cells specific for WT1 can kill cells that express WT1 protein. Introduction of genes encoding T-cell receptor (TCR) chains for WT1 are used as a means to quantitatively and qualitatively improve response to WT1 bearing leukemia and cancer cells" (e.g. column 26, last paragraph). Non-specific T cells can be transfected with a polynucleotide encoding TCRs specific for a polypeptide described herein to render the host cell specific for the polypeptide. The hose cells can be used for adoptive immunotherapy of WT associated cancer (e.g. column 28, 1st paragraph).

Nishimura teaches that it is difficult to maximize activation of antitumor immunity in vivo only by MHC class I-associated peptide, activation of class II-restricted helper T (Th) cells

is also required for induction of CTL which has recognized class I-associated tumor peptide (e.g. p. 363 (2-1 in the submitted copy filed 10-12-06).

It would have been prima facie obvious for one of ordinary skill in the art at the time of the invention to transduce Th cells or both Th1 and Tc1 cells with a TCR gene for WT1 because Tsuji teaches transducing Tc1 cells with a retrovirus expressing 2C TCR gene, which is a class I-restricted TCR, and Gaiger teaches transducing T cells with a gene encoding TCR chains for WT1. T cells encompass Th cells and Tc cells and Nishimura shows that activation of class II-restricted helper T cells is required for induction of CTL (Tc cells) which ahs recognized class I-restricted tumor peptide. It would be obvious for one of ordinary skill in the art to transducer Th cells or both Th1 cells and Tc1 cells with gene encoding TCR chains for WT1 in view of the teaching of Tsuji, Gaiger and Nishimura. It would be obvious for one of ordinary skill in the art to transducer T cells with gene for class II-restricted TCR because Nishimura shows that activation of class II-restricted helper T cells is required for induction of CTL (Tc cells) which ahs recognized class I-restricted tumor peptide. It also would have been obvious for one of ordinary skill in the art to separate the Th cells or Th1 and Tc1 cells with antibody-bearing magnetic beads or mixing separated Th1 cells and Tc1 cells in any proportion because it was known in the art to use antibody-bearing beads to separate cells with different antigen on the cell surface and determining various mixing proportion of Th1 cells and Tc1 cells would be routine optimization of a result effective variable.

One having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to generate 2C-TCR gene-modified antigen specific Tc1 cells for exhibiting antitumor activity as taught by Tsuji and producing T cells expressing TCR specific

for WT1 polypeptide for adoptive immunotherapy of WT associated cancer as taught by Gaiger with reasonable expectation of success.

Information Disclosure Statement

11. The information disclosure statement (IDS) was submitted on 10-12-06 and 4-23-08. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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